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14. ABSTRACT Using fMRI, we are conducting an observational study to characterize the pattern of brain activation during performance of cognitive control and working memory tasks in service personnel with mild traumatic brain injury (TBI) and severe TBI imaged between 3 and 42 months after injury. Presently in this work, we are standing by to begin patient recruitment and data collection at Walter Reed Army Medical Center (WRAMC). There are two administrative matters remaining to be resolved before we are authorized to collect data from human participants. These are WRAMC Commanding Officer endorsement on a submitted DoD Institutional Agreement for IRB Review between WRAMC and the Naval Medical Research Center (NMRC) and completed CDMRP review of the fully endorsed protocol. The ongoing research by our study partner, Dr. Harvey Levin has produced meaningful data and significant published results for patient populations with TBI not associated with blast. As an extension of Dr. Levin's successful research model, we anticipate that the contributions from our present study, specifically the addition of a patient group with severe TBI associated with blast, will uniquely complement and augment these research findings.					
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## INTRODUCTION

Blast-induced neurotrauma is not well documented in medical research literature, partly because conventional brain imaging techniques provide sparse information concerning the neural substrate of associated deficits and implications for rehabilitation. Novel brain imaging techniques provide promise for increasing neuroimaging sensitivity in this patient population. Specifically, functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) represent opportunities for enhancing utility of imaging in the study of this injury, including rehabilitation. Using fMRI, we are conducting an observational study to characterize the pattern of brain activation during performance of cognitive control and working memory tasks in service personnel with mild traumatic brain injury (TBI) and severe TBI imaged between 3 and 42 months after injury. DTI is applied as a method of enhanced assessment of the neural mechanisms underlying cognitive and behavioral sequelae of TBI in this patient population (e.g., reference 1).

## BODY

Presently in this work, we are standing by to begin patient recruitment and data collection at Walter Reed Army Medical Center (WRAMC). There are two administrative matters remaining to be resolved before we are authorized to collect data from human participants. These are WRAMC Commanding Officer endorsement on a submitted DoD Institutional Agreement for IRB Review (IAIR) between WRAMC and the Naval Medical Research Center (NMRC) and completed CDMRP review of the fully endorsed protocol.

Although we have not yet been able to collect data from human participants, several of the goals described in our statement of work have been achieved.

- Investigator meetings: Our first Investigator meeting was held in Houston, Texas during a 2-day workshop at Baylor College of Medicine in August 2008. Here, we reviewed the aims and status of the project and discussed the neuropsychological measures and procedures. We also discussed patient recruitment, MRI and DTI scan protocols, quality assessment procedures, safety, data management and transfer procedures, the fMRI tasks, and analysis procedures. These discussions included training on each aspect of procedures in this research; this discussion and training was of critical importance as a target of this

research is data comparability between data sets collected by 2 different labs in Washington, DC and in Houston, TX. Our second meeting is scheduled in Kansas City, Missouri in August 2009.

- Study manual: Revisions to the study manual were completed in October of 2008 and were submitted to WRAMC DCI as an element of the research protocol.
- Data de-identification: In September 2008 we developed a series of procedures for the removal of protected health information from MRI data sets. These procedures will be followed to de-identify data sets prior to their distribution to our study partners at Baylor College of Medicine.

Some delay in our progress occurred at the outset of this work when the annual IRB Continuing Review of our extant protocol at the National Institutes of Health (NIH), which supports our MRI scans of military personnel with TBI, was unexpectedly directed for significant revision and resubmission for full IRB review. Following major revisions, the protocol was resubmitted and then approved on 10 October 2008.

#### KEY RESEARCH ACCOMPLISHMENTS

- Coordination with other TBI research groups at WRAMC: We have helped organize a monthly meeting with other research groups at WRAMC who have active or pending protocols in TBI research. These meetings have already better positioned our research for effective recruitment of WRAMC patients who meet protocol eligibility criteria. This meeting/dialogue series will become increasingly important as additional TBI research protocols are approved at WRAMC. The primary goals of these meetings:
  - Familiarize the different research groups with the other study designs.
  - Coordinate patient recruitment to equitably enroll patients without overburdening patients and staff.
  - Discuss the progress of all the existing and upcoming TBI protocols.
  - Avoid redundant or conflicting administration of tests and measures to participants.
- Met with Outpatient Program Coordinator at NIH to discuss the logistics and procedures for admitting WRAMC TBI patients to NIH: Topics discussed included the scheduling of procedures, meals for patients, escorts at the NIH hospital, and patient transport to and from NIH.

- 2-day workshop for study investigators in August 2008: Including Baylor College of Medicine, Michael E. DeBakey Veterans Affairs Medical Center, Brooke Army Medical Center, and Naval Medical Research Center.
- Adaption of MRI tasks: The tasks administered to participants during the MRI scans were originally written to operate with the IFIS-SA fMRI system in place at the Michael E. DeBakey Veterans Affairs Medical Center. It was necessary to re-write the computer scripts that drive these tasks to operate on a standard laptop and response devices, as will be used at NIH.
- Test scans (fMRI and DTI) on a phantom were conducted with the General Electric 3T MRI to be used at the NIH NMR Center: These test scans used parameters adapted from those in use by Dr. Levin's team using a Philips 3T MRI. The data collected were then analyzed to determine scan sequence and result comparability.
- Research protocol pre-reviewed at CDMRP: The primary research protocol was submitted to a pre-review by a Human Subjects Protection Scientist (HSPS) from the United States Army Medical Research and Materiel Command (USAMRMC), Office of Research Protections (ORP), Human Research Protection Office in June 2008 and changes to the protocol were made in accordance with that review.
- The NIH protocol was rewritten and approved by NIH IRB in October 2008.
- WRAMC Department of Clinical Investigation (DCI) scientific review: The protocol was submitted for review and assigned a WRAMC DCI identifier (#7046) in October 2008 and DCI committee met in December 2008 and accepted the revised protocol in January 2009.
- NMRC scientific review: The protocol was submitted to the NMRC scientific review board (SRB) in October 2008 and was assigned protocol identifier NMRC.2009.0002. It was approved by NMRC SRB in November 2008.
- WRAMC DCI Human Use Committee (HUC) review: The WRAMC HUC considered this protocol in January 2009 and protocol revisions were reviewed and accepted by the HUC in February 2009.
- Clinical Investigation Regulatory Office (CIRO) review: The protocol was submitted to CIRO by WRAMC DCI in February 2009 and approved in March 2009.

#### REPORTABLE OUTCOMES

None.

## CONCLUSION

The ongoing research by our study partner, Dr. Harvey Levin has produced meaningful data and significant published results for patient populations with TBI not associated with blast. As an extension of Dr. Levin's successful research model (e.g., references 2-7), we anticipate that the contributions from our present study, specifically the addition of a patient group with severe TBI associated with blast, will uniquely complement and augment these research findings.

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